and said immobile indicator capture reagent is capable of binding to said extracted antigen-indicator labeling reagent complex;

(c) forming an extracted antigen-indicator labeling reagent complex; and

(d) determining the presence or absence of said antigen in the sample by the presence or absence of a signal formed by the binding of said extracted antigen-indicator labeling reagent complex to said indicator capture reagent specific for said extracted antigen-indicator labeling reagent complex.

DRAWINGS

Applicants will delay filing of new formal drawings until after receipt of the "Notice of Allowability" (PTO-37).

REMARKS

This invention relates to one-step immunoassays for extracted analytes which can be performed by individuals without extensive training in laboratory techniques. This invention further relates to immunoassays for the detection of extracted analytes which permit efficient extraction while minimizing sample manipulation following extraction.

These assays do not require a complex plastic or cardboard housing or specially designed swabs to fit in the complex housings. In addition, the claimed immunoassays for an extracted antigen do not require transfer of the sample containing the extracted

antigen to the immunoassay device. This invention further relates to one-step immunoassays for a Strep A antigen in which the Strep A antigen is efficiently extracted from samples using 2 or less sample extraction reagents which can be added to the sample in any sequence.

Claims 1-8 are pending. Claims 1-8 have been rejected as indefinite. Claims 1, 2, 4 and 6-8 have been rejected as anticipated by Imrich et al. (U.S. Patent No. 5,415,994). Claims 3 and 5 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Imrich et al. in view of Bogart et al. (U.S. Patent No. 5,494,801) and Murray (U.S. Patent No. 3,957,436). Claim 9 is new.

Correction of Informalities

Applicants have amended the specification to correct informalities noted by the Examiner. Applicants believe that one of ordinary skill in the art would have known the full name for EDAC, MES and GAS and that amendment to add these full names does not constitute new matter. (See, e.g., pages from the attached Sigma catalog referring to 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide as EDAC, and to 2-(N-morpholino)ethanesulfonic acid as MES. See also page 65 of the specification which refers to the full name for "GAS", which is "Group A Streptococcus").

The Examiner has also indicated that "[t]here are no detailed descriptions of Figures 5, 6, 7, 8(a)-(c) and 9(a)-(c)." [Office action mailed 3/23/98 at page 4]. Descriptions of figures 5, 6, 7, 8(a)-(c) and 9(a)-(c) are set forth at page 43, line 9 to page 44, line 23. Applicants respectfully assert that these "brief" descriptions are set

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forth in sufficient detail to permit one of ordinary skill in the art to understand the relevance of the figures to the claimed invention.

Trademark Usage

The specification has been amended to indicate use of the TWEEN 20™ trademark when referring to TWEEN 20™ detergent.

Claim 9

Claim 9 has been added. It is substantially similar to Claim 1 except that it is directed to an assay to detect a Streptococcus antigen. Support therefor is found at page 29, line 13 to page 30, line 4 where the term analyte is described as follows:

> Analyte can include any antigenic substances, haptens, antibodies and combinations thereof. The analyte of interest in an assay can be, for example, a protein, a peptide, an amino acid, a nucleic acid, a hormone, a steroid, a vitamin, a pathogenic microorganism for which polyclonal and/or monoclonal antibodies can be produced, a natural or synthetic chemical substance, a contaminant, a drug including those administered for therapeutic purposes as well as those administered for illicit purposes, and metabolites of or antibodies to any of the above substances.

35 U.S.C. § 112

The Examiner has indicated that the language "may be added" recited in claim 1 is indefinite. Applicants believe that the rejection is no longer applicable in light of Applicants' amendment to more clearly recite that the said two reagents "are added to said assay chamber in no particular sequence".

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The Examiner has further indicated that use of the terms "comprising", "containing" and "having" are unclear, with respect to whether a difference exists between the terms. Applicants believe that this rejection is no longer applicable in view of the amendment of the claims to replace the terms "containing" and "having" with "comprising".

The Examiner has also rejected claim 1 as vague and indefinite in reciting "introducing". Applicants respectfully assert that one of ordinary skill in the art would understand that the term "introducing" can refer to any method of bringing the sample receiving region of a lateral flow immunochromatographic device into contact with the extracted mixture of step (a), for example, inserting the sample receiving region of a lateral flow immunochromatographic device into the extracted mixture of step (a); or capping a test tube containing the extracted mixture of step (a) with a cap which has a lateral flow device mounted at a perpendicular angle to the inner surface of the lid (with the sample receiving region closest to the lid), such that when sealed, the device extends into the test tube but does not contact the mixture--after sufficient time has passed for efficient extraction, the tube can inverted to bring the extracted mixture of step (a) into contact with the sample receiving region of the lateral flow immunochromatographic device. See page 30, line 9 to page 31, line 11.

Next the Examiner asserts that claim 1 is indefinite with respect to the antecedent basis for "said sample"; failing to provide reagents for "forming an antigen-indicator labeling reagent complex"; reciting "antigen" and extracted antigen" interchangeably; and for failing to disclose structural elements of the

immunochromatographic device. [Office Action mailed 3/23/98, at pages 5 & 6]. Applicants believe that these rejections are no longer applicable in view of amendments of claim 1 to more clearly recite the order of steps (a)-(d), to refer to the antigen as the "extracted antigen" when referring to the antigen after the extraction step (a) has been performed, and to recite structural elements of the lateral flow immunochromatographic device. Support for those amendments is found at page 23, line 6 to page 24, line 11, and at page 25, lines 19-23.

Similarly, Applicants believe that amendment to claim 2 to more clearly recite reagents and structures involved in the formation of a positive control signal overcome the Examiner's rejection of claim 2 as indefinite. Support for the amendment is found at page 23, line 17 to page 25, line 10; page 25, lines 19-23; and page 35, line 20 to page 36, line 21.

Claim 4 has been amended to delete the term "further" because the composition of the extraction reagents had not been previously recited. Applicants therefore believe that the Examiner's rejection of claim 4 as indefinite is no longer applicable.

The Examiner has also rejected claim 5 as indefinite for failing to recite a means for a color change. Applicants believe that this rejection is no longer applicable in light of the amendment of claim 5 to more clearly recite the presence of a color indicator reagent. Support therefor is found at page 21, lines 2-11. One of ordinary skill in the art would be aware of various color indicators which could be added to a solution of sodium nitrate to form a colored solution which will change colors when mixed with acetic acid.

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35 U.S.C. § 102

The Examiner has rejected claims 1, 2, 4, and 6-8 under 35 U.S.C. § 102(b) as anticipated by Imrich et al. (U.S. Patent No. 5,415,994). [Office Action mailed 3/23/98 at pages 7-8]. Imrich describes immunoassays using devices with complex plastic housings in which the extraction chamber is in fluid contact with the sample receiving zone of the immunoassay device. [See col. 4, lines 24-37]. Upon introduction of the extraction reagents into the extraction chamber, the extraction reagents contact the (swab) sample and can immediately flow onto the sample receiving region of the immunoassay device.

In order to anticipate a claim, a reference must disclose every element of a claim. Minnesota Min. and Mfg. v. Johnson & Johnson, 976 F.2d 1559, 1565 (Fed. Cir. 1990); see Credle v. Bond, 25 F.3d 1566, 1578 (Fed. Cir. 1994). However, because Imrich discloses methods utilizing an immunoassay device in which the extraction chamber is in fluid contact with the sample receiving region of the immunoassay device, Imrich fails to disclose the step of introducing the sample receiving region of a lateral flow immunochromatographic assay device into the extraction reagents containing the extracted antigen after the extraction step has taken place. Applicants therefore respectfully assert that Imrich does not anticipate claims 1, 2, 4, and 6-8. Moreover, Imrich contains no suggestion that the assays may be carried out by introducing the immunochromatographic device into the extraction reagent mixture containing the extraction antigen after the extraction has taken place, without further manipulation of the sample. Introduction of the device into the extraction reagent mixture containing

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the extraction antigen after extraction permits efficient extraction to take place before the sample is placed in fluid contact with the lateral flow immunoassay device. Moreover, introduction of the device into the extraction reagent mixture eliminates the need for additional manipulation of the sample after the extraction step, so that extensive training in laboratory techniques is not required to perform the assays of this invention. Applicants therefore respectfully assert that Imrich also does not make obvious claims 1-8.

Moreover, Imrich fails to teach the use of a test strip without a housing containing an extraction chamber, and therefore does not anticipate or make obvious claim 7, which is directed to methods using a test strip without a plastic housing.

35 U.S.C. § 103(a)

The Examiner has rejected claims 3 and 5 under 35 U.S.C. § 103(a) as unpatentable over Imrich et al. in view of Bogart et al. (U.S. Patent No. 5,494,801) and Murray (U.S. Patent No. 3,957,436). As set forth above, Imrich discloses the use of devices containing complex plastic housings, and does not disclose the step of introducing the sample receiving region of a lateral flow immunochromatographic assay device into the extraction reagents containing the extracted antigen, after the extraction step has been performed. Moreover, neither Bogart et al. nor Murray et al. contain any suggestion to introduce the immunoassay device into the extraction mixture following extraction, without further manipulation of the sample. Murray et al. does not describe the use of lateral flow assay devices at all, while Bogart et al. describes only assays

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involving further manipulation of the extracted sample in order to bring the extracted sample in contact with a test surface. [See e.g., Bogart et al. at col. 9, lines 39-45; col. 11, line 66-col. 12, line 2; col. 15, lines 31-34]. Therefore, there would have been no motivation to combine the immunoassays of Imrich et al. with the extraction procedure of Bogart et al. or the use of a color indicator described in Murray et al. to obtain the claimed methods. "The motivation to combine references can not come from the invention itself." Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 U.S.P.Q.2d 1377, 1380 (Fed. Cir. 1993). Applicants therefore respectfully assert that claims 3 and 5 are not made obvious by Imrich et al. in view of Bogart et al. and Murray et al.

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CONCLUSION

Applicant believes that claims 1-8 are in condition to be allowed and respectfully request that they be allowed and passed to issue. Although Applicant believes no fee is due for filing this response, if any fee is due for the prosecution of this matter, the Patent Office is hereby authorized to debit Deposit Account No. 12-2475.

Respectfully submitted,

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